REMARKS

Applicants submit the Abstract on a separate sheet, for inclusion in the instant application. Please add this as the last page of the application. Applicants have made amendments and cancellations to the claims in order to pursue a preferred embodiment of the invention at this time. Claims 1, 4, 5, 7, 9-11, 15, and 22 have been amended, claims 2, 3, 6, 12-14, 18, and 19 have been canceled, and new claims 27-33 have been added.

Support for amendment of the claims and the new claims can be found throughout the specification and originally filed claims. More specifically:

Support for amendment of claim 1 is found, for example, at paragraphs [005], [037], and [063].

Support for amendment of claim 4, 7 and 9 is self evident.

Support for amendment of claim 5 is found, for example, in original claim 6.

Support for amendment of claim 10 is found, for example, at paragraph [0063].

Support for amendment of claims 11 and 15 is found, for example, at paragraph [005].

Support for amendment of claim 22 is found, for example, at paragraph [037], and [063].

Support for new claim 27 is found, for example, at paragraph [107].

Support for new claim 28 is found, for example, at paragraph [003], and [037].

Support for new claim 29-31 is found, for example, at paragraph [0037].

Support for new claim 32 is found, for example, at original claim 4.

Support for new claim 33 is found, for example, at paragraph [0063].

Applicants respectfully request entry of the amendments and new claims.

Objections to the Specification

The Examiner has objected to the specification as having the Abstract of the Disclosure in an inappropriate place. In response, Applicants have submitted the abstract on a separate sheet to be included in the application as the last page of the application. This submission obviates the objection to the specification.

Rejection of Claims under 35 USC 112, First Paragraph

Claims 1-26 have been rejected under 35 USC 112, first paragraph, as not enabled by the specification. Applicant submits that independent claim 1 has been amended to recite "a method of treating a neurological disorder of the eye in a subject in need thereof comprising administering to the subject a therapeutically effective amount of D-mannose to produce a neurosalutary effect within the eye." Independent claim 22 has been amended to recite "a neurological disorder of the eye". The Examiner has stated that the specification is enabling for the regeneration of axons on rat retinal ganglion cells from the administration of D-mannose and forskolin. Applicant submits that the rat retinal ganglion cell regeneration assay used in Applicants' experiments provide an accepted *in vitro* model for *in vivo* neuronal regeneration within the mammalian eye. Applicants submit that the ordinary skilled artisan would be able to perform the invention recited in the amended claims from the guidance presented in the specification and available in the art at the time of the invention, through no more than routine experimentation. With respect to the alleged requirement of concurrent administration of cAMP modulator with the D-mannose, Applicants submit that the ordinary skilled artisan is aware that circumstances exist in which the *in vivo* levels of **endogenous** cAMP are sufficient to promote the activity of exogenously added D-mannose. As such, the addition of an exogenous cAMP modulator is not a requirement in all circumstances. Determination of circumstances which require the addition of exogenous cAMP is within the ability of the ordinary skilled artisan through routine experimentation. As such, Applicant's claims as amended are enabled by the specification.

Rejection of Claims under 35 USC 112, Second Paragraph

Claims 4-7 and 26 have been rejected under 35 USC 112, second paragraph as being indefinite. More specifically, claim 4 has been rejected for its recitation of "membrane depolarization" since all other terms recited in the Markush group are compounds, while "membrane depolarization is an effect produced. To clarify Applicants intention, claim 4 has been amended to omit the term "membrane depolarization". New claim 32 has been submitted which recites that the cAMP modulator functions by causing membrane depolarization, as originally intended by inclusion of the term in original claim 4. Applicants submit that this amendment obviates the rejection and respectfully request its withdrawal.

Claim 5 has been rejected for its recitation of "a macrophage derived factor". Applicants submit that the term "macrophage derived factor" is defined in the specification at page 9, paragraph [0030] as including any factor derived from a macrophage that has the ability to produce a neurosalutary effect in a subject. Examples of such a macrophage derived factor are set forth as TGF-B and oncomodulin. However, in an effort to expedite prosecution, this term has been omitted from the claim. Applicants submit that this rejection has been obviated by the amendment and respectfully request its withdrawal.

Claim 26 has been rejected as unclear as to what the term "further comprising oncomodulin" means. Applicants submit that the claim as it reads is clear. The Application does not indicate to the ordinary skilled artisan that oncomodulin is a cAMP modulator. Rather, the application indicates that oncomodulin is a macrophage derived factor. The Examiner is perhaps confusing the term "a macrophage derived factor" which is indicated in the Application as including oncomodulin, with the term "a macrophage derived factor that stimulates cAMP". The two terms are not equivalent. The ordinary skilled artisan would recognize that not all macrophage derived factors stimulate cAMP. Further, the ordinary skilled artisan knows that oncomodulin is not used in the art or generally referred to as a cAMP modulator. In light of this, Applicants submit that the claims are clear and respectfully request withdrawal of this rejection.

Double Patenting Rejections

Claims 1-21 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 31-32 and 34-37 of copending Application No. 10/580,364 ('364). In the rejection, the Examiner contends that, although the instant claims and the '364 claims differ since the instant claims do not employ an NgR antagonist, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the method of '364 since both are used for treatment of neurological disorders.

Applicants respectfully traverse this rejection and submit that the instant claims are patentably distinct over those of '364 precisely because the instant claims do not specify administration of an NgR antagonist. The subject claims of the '364 application are limited to require an NgR antagonist **and** an agent that activates the growth pathway of CNS neurons, with dependent claims reciting that the agent that activates the growth pathway can be a hexose. Nowhere in the claims of the '364 application is it taught or suggested that the hexose alone, i.e., in the absence of an NgR antagonist, would have a beneficial or therapeutic effect. Because the claims of the '364 application hinge upon the **combination** of an NgR antagonist and the other agent, without some express teaching or suggestion to omit the NgR antagonist, one cannot say that it would be obvious to do so, nor would it be obvious that administering the other agent (which can encompass a hexose) alone would have any beneficial effect. The Office Action states "The use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed method unobvious over the prior art." This is incorrect as applied to the instant claims, because the instant claims do **not** simply use a known member of a class of agents in a method to effectuate the same type of treatment, but rather, **omit** an agent taught to be *required* in the claims of the '364 application. Reconsideration and withdrawal of the provisional obviousness-type double patenting rejection over claims of the '364 application is respectfully requested.

Applicants further note that because the cited co-pending application has a later priority date than the present application, in all likelihood, a patent which issues from the instant application will expire before a patent that issues from the '364 application. Therefore, a

terminal disclaimer of the patent term extending beyond the term of any '364 issued patent is unnecessary.

Claims 22-26 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 18-20 and 22 of co-pending Application No. 11/804,295 ('295). Applicant requests that this rejection be held in abeyance until an indication of allowable subject matter.

Claims 1-6, 10, 15-17 and 21-22 have been rejected on the ground of obviousness-type double patenting as unpatentable over claims 1-4, 7-10 and 12-13 of U.S. Patent no. 6,855,690 ('690). Applicants assume that in this rejection, the Examiner meant to reject, claims 20-21, rather than claims 21-22, since claim 22 is an independent claim which does not directly relate to the subject matter being discussed in this rejection, while claim 20 depends from rejected claim 10 and does directly relate to the subject matter at hand. Applicants respectfully traverse this rejection.

The subject claims of the '690 patent are limited to require oncomodulin. Nowhere in the claims of the '690 patent is it taught or suggested that D-mannose, in the absence of oncomodulin, would have a beneficial or therapeutic effect. Because the claims of the '690 patent hinge upon the requirement of oncomodulin, without some express teaching or suggestion to omit the oncomodulin from the claimed methods, one cannot say that it would be obvious to do so, nor would it be obvious that administering an agent recited in the dependent claims (e.g. mannose) alone would have any beneficial effect. The Office Action states "The use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed method unobvious over the prior art." This is incorrect as applied to the instant claims, because the instant claims do **not** simply use a known member of a class of agents in a method to effectuate the same type of treatment, but rather, **omit** an agent taught to be *required* in the claims of the '690 patent. Similarly, the instant claims are limited to require D-mannose. The instant claims neither teach nor suggest use of oncomodulin in the absence of mannose. Nowhere in the instant claims is it taught or suggested that oncomodulin, in the absence of D-mannose, would have a beneficial or therapeutic effect. As such, the rejection is improper. Reconsideration and withdrawal of the provisional obviousness-

type double patenting rejection over claims 1-4, 7-10 and 12-13 of the '690 patent is respectfully requested.

Claims 22-26 have been rejected on the ground of obviousness-type double patenting as unpatentable over claims 1 and 2 of U.S. Patent no. 7,238,529 ('529). Applicants assume that this is not a provisional rejection, since it is made over claims of an issued U.S. Patent.

Applicants respectfully traverse this rejection. The subject claims of the '529 patent are limited to require oncomodulin with an axogenic factor such as mannose. Applicants claims 22, 23, and 25 contain no such limitation. The Office Action states "the use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed composition unobvious over the prior art." This is incorrect as applied to the instant claims, because the instant claims do **not** simply use a known member of a class of agents in a method to effectuate the same type of treatment, but rather, **omit** an agent taught to be *required* in the claims of the '529 patent. The subject claims of the '529 patent neither teach nor suggest omission of oncomodulin from the claimed composition. Without some express teaching or suggestion to omit the oncomodulin from the claimed composition, one cannot say that it would be obvious to do so. As such, the rejection is improper. Reconsideration of the claims and withdrawal of the rejection is respectfully requested.

Rejection of Claims under 35 USC 102

Claim 22 has been rejected under 35 USC 102(b) as anticipated by Sherman et al. (U.S. 4,471,114). In the Office Action, the Examiner states that "Sherman teaches an effluent which comprises an aqueous solution of D-mannose. This reads on instant claim 25." In a phone call with Applicants' attorney, the Examiner indicated that the recitation of claim 25 in the rejection was the result of a typographical error, and that his intention was to reject claim 22. In the rejection, the Examiner contends that even though Sherman does not teach the composition in a packaging material as instantly claimed, it is within the skill level of the artisan to package such a composition with a label. Applicants respectfully traverse this rejection. For a reference to anticipate a claim it must teach **every element of the claim**. Claim 22, as amended, recites:

> An article of manufacture comprising packaging material and a pharmaceutical agent contained within said packaging material, wherein said packaging material comprises a

label which indicates said pharmaceutical may be administered, for a sufficient term at an effective dose, for treating a neurological disorder of the eye together with a pharmaceutically acceptable carrier, wherein the pharmaceutical agent comprises D-mannose.

Applicants submit that Sherman does not teach an article of manufacture comprising D-mannose. Nor does Sherman teach an article of manufacture comprising packaging material which comprises a label which indicates the pharmaceutical agent therein can be administered for treating a neurological disorder (of the eye). Because the cited art of Sherman does not teach every element of the rejected claim, this rejection is improper. As such, Applicants respectfully request withdrawal of this rejection.

Applicants further submit that claim 22 is not obvious over Sherman since nothing in Sherman suggests an article of manufacture comprising D-mannose, and nothing in Sherman suggests an article of manufacture comprising packaging material which comprises a label which indicates the pharmaceutical agent therein can be administered for treating a neurological disorder (of the eye).

In view of the amendments to the claims and the arguments presented above, Applicants respectfully submit that the claims are now in condition for allowance.

The Commissioner is authorized to charge any fees and credit any overpayments that may be due in connection with this submission to Nixon Peabody LLP Deposit Account No. 50-0850.

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Respectfully submitted,

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